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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/575,905	04/30/2007	Kunihiro Hattori	14875-161US1 C1-A0313P2-U	2076

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EXAMINER	
OUSPENSKI, ILIA I	

ART UNIT	PAPER NUMBER
1644	

NOTIFICATION DATE	DELIVERY MODE
06/23/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PATDOCTC@fr.com

Office Action Summary	Application No.	Applicant(s)	
	10/575,905	HATTORI ET AL.	
	Examiner	Art Unit	
	ILIA OUSPENSKI	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 April 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,4-20,22-36 and 38* is/are pending in the application.

4a) Of the above claim(s) *20,23-36 and 38* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,4-7,12-19 and 22* is/are rejected.

7)☒ Claim(s) *8-11* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *14 April 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/3/07; 2/11/08; 5/29/08; 1/8/09; 9/25/09; 4/16/10*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment and remarks filed on 04/16/2010 are acknowledged.

Claims 2, 4-20, 22-36 and 38 are pending.

2. Applicant's election with traverse of Group II (claims 2, 4 – 19 and 22, drawn to a bispecific antibody that has an activity of functionally substituting for a ligand of a heteromolecule-comprising receptor, in particular an antibody comprising an anti-AR2 chain comprising SEQ ID NOS: 9 and 10, and to compositions and kits comprising said antibody) in the reply filed on 04/16/2010 is acknowledged. Applicant further elected the species wherein the anti-AR1 chain comprises SEQ ID NOS: 1 and 2.

The traversal is on the grounds that the cited reference of Ledbetter et al. allegedly does not anticipate claim 2 as unamended.

Applicant's arguments do not address the merits of the restriction requirement as it applies to unamended claims; consequently the requirement is still deemed proper and is therefore made FINAL.

In the interest of compact prosecution, examination has been extended to include the species wherein the anti-AR1 chain comprises SEQ ID NOS: 3 and 4.

Claims 20, 23-36 and 38 are withdrawn from further consideration by the Examiner, under 37 C.F.R. § 1.142(b), as being drawn to nonelected inventions, there being no allowable generic or linking claim.

Claims 2, 4 – 19 and 22 are presently under consideration.

3. Claims 10 and 11 are objected to as reading on non-elected embodiments of the invention, which are not under consideration in the instant application. Applicant is required to cancel the non-elected embodiments.

4. The following is a quotation of the **second paragraph of 35 U.S.C. 112**.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claim 22 is rejected under **35 U.S.C. 112, second paragraph**, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 22 is indefinite in the recitation of "a method" in the absence of setting forth any method steps. Therefore, one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the claimed invention.

Applicant is reminded that any amendment must point to a basis in the specification so as not to add new matter. See MPEP 714.02 and 2163.06.

6. The following is a quotation of the **first paragraph of 35 U.S.C. 112**:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 2, 4 – 7, 12 – 19 and 22 are rejected under **35 U.S.C. 112, first paragraph**, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Applicant is not in possession of the claimed bispecific antibody, because Applicant is not in possession of the generically recited "ligand" or a generically recited "heterodimeric receptor."

The instant specification discloses non-limiting examples of "ligands" and "heterodimeric receptors," however, these are not seen as sufficient to place Applicant in possession of the respective genera, because the exemplary ligands and receptors are diverse in their structures and functions, and furthermore because the genera encompass members which are distinct in structures and functions from those disclosed, including possible ligands and receptors which are yet to be discovered. In the absence of a disclosure in the instant specification of sufficiently detailed, relevant identifying characteristics, such as complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics, the skilled artisan cannot envision all the contemplated ligands and receptors encompassed by the instant claims, based upon the disclosure provided in the specification as-filed.

Adequate written description requires more than a mere statement that it is part of the invention. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993). The Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, §1 "Written Description" Requirement make clear that if a claimed genus does not show actual reduction to practice for a representative number of species; then the Requirement may be alternatively met by reduction to drawings, or by disclosure of

relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 column 3).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398. Applicant is directed to the Guidelines for the Examination of Patent Applications under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, January 5, 2001.

8. Claims 13 – 19 and 22 are rejected under **35 U.S.C. 112, first paragraph**, as failing to comply with the enablement requirement. The claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention.

The specification does not provide a sufficient enabling description of a composition for "preventing and/or treating" any diseases.

The specification does not enable one of skill in the art to make and use the invention as claimed without undue experimentation. Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized in In re Wands (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, limited working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention.

In evaluating the facts of the instant case, it is noted that in applying therapies based on T cell costimulatory molecules, in vitro and even animal model studies have not correlated well with in vivo clinical trial results in patients. Since the efficacy of therapeutic antibodies can be species- and model-dependent, it is unpredictable whether reliance on the considerations described in the instant specification provide the basis for employing the recited antibodies for treating any diseases. For example, Blazar et al. (J. Immunol., 1996, 157: 3250 – 3259; see entire document, in particular, e.g. page 3257, column 2 first paragraph) disclose that issues such as tissue distribution, half-life, affinity and avidity obtained with various reagents targeting immunoregulatory molecules might prove to be highly important in achieving a therapeutic effect. Therefore, any conclusion regarding the efficacy of immune modulation on altering in vivo immune response should be interpreted in light of the specific reagent used (Blazar et al., see page 3257, column 2, paragraph 1). Thus there is no evidence that the animal model used in the experiments disclosed in the specification would be predictive of the therapeutic methods encompassed by the claims.

Pharmaceutical therapies in the absence of in vivo clinical data are unpredictable for the following reasons; (1) the protein may be inactivated before producing an effect, i.e. such as proteolytic degradation, immunological inactivation or due to an inherently short half-life of the protein; (2) the protein may not reach the target area because, i.e.

the protein may not be able to cross the mucosa or the protein may be adsorbed by fluids, cells and tissues where the protein has no effect; and (3) other functional properties, known or unknown, may make the protein unsuitable for in vivo therapeutic use, i.e. such as adverse side effects prohibitive to the use of such treatment. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

Further, the burden of enabling the prevention of a disease is greater than that of enabling a treatment method due to the need to screen the subjects susceptible to the respective condition and the difficulty of proof that the administration of the drug was the agent that acted to prevent the condition. The specification does not provide guidance as to how one skilled in the art would go about screening those patients susceptible to any diseases within the scope of the presently claimed invention. Nor is guidance provided as to a specific protocol to be utilized in order to prove the efficacy of the presently claimed compounds in preventing these disease states. Accordingly, undue experimentation is necessary to determine screening and testing protocols to demonstrate the efficacy of the presently claimed invention.

In view of insufficient guidance by the instant specification and the lack of predictability of the art to which the invention pertains with respect to the therapeutic efficacy of the claimed antibodies, undue experimentation would be required to make the claimed compositions with a reasonable expectation of success in using them for treatment or prevention of the recited diseases, absent a specific and detailed description in applicant's specification of the clinical protocols, and absent working examples providing evidence that the claimed methods are effective for treating any of the recited pathological conditions.

9. Claims 8 and 9 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claims 10 and 11 are objected to for the reasons set forth in section 3 supra, and further as being dependent upon a rejected base claim, but would be allowable if limited to the elected invention rewritten in independent form including all of the limitations of the base claim and any intervening claims.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ILIA OUSPENSKI whose telephone number is (571)272-2920. The examiner can normally be reached on Monday-Friday 9 - 5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram R. Shukla can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/ILIA OUSPENSKI/
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Primary Examiner
Art Unit 1644
June 17, 2010